UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDE, AND TOXIC SUBSTANCES

February 2, 2010

MEMORANDUM

SUBJECT: Decision Document for Petition Number 8E7402;
Ammonia salts of higher fatty acids (C_8-C_{18} saturated)

FROM: Deirdre Sunderland, Industrial Hygienist
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

TO: PV Shah, Chief
Inert Ingredient Assessment Branch (IIAB)
Registration Division (7505P)

EXCUTIVE SUMMARY

A petition requesting an exemption from the requirement of tolerance for ammonium salts of fatty acids (C_8-C_{18} saturated) under 40 CFR 180.910 was submitted to the Environmental Protection Agency, herein referred to as the Agency or EPA, by Falcon Lab, LLC.

Ammonium salts of fatty acids are mineral salts of naturally occurring fatty acids found in the environment. Fatty acids play a significant role in the normal diet of humans, animals, and plants and currently have FDA and EPA approved uses in food products. They are also found in cosmetics and household cleaners.

Ammonium salts of fatty acids have shown to be of low toxicity via the oral and dermal routes of exposure, Toxicity category IV and III, respectively (40 CFR 156.62). When applied for long periods of time, they have the potential to be dermal irritants. Ammonium salts of fatty acids are eye irritants and have the potential to cause permanent eye injury. Limited data are available regarding the inhalation toxicity of soap salts; however, they are anticipated to be irritating via the inhalation route of exposure.

A subchronic range finding study did not see any significant systemic toxicity of nonanoic acid (C_9 saturated) given to rats at doses up to 1,834 mg/kg/day. Ammonium salts of fatty acids are not believed to be mutagenic.

When used at high doses, reproductive and mutagenic effects were observed in laboratory animals given potassium salts of coco fatty acids; however, studies on one of the ammomium salts, pelargonic acid (nonanoate acid), did not show developmental or mutagenic effects. Due to the lack of mutagenicity, the low toxicity, and the anticipated exposure from the use of these chemicals as inert ingredients in pesticide products the Agency does not believe ammonium salts of fatty acids (C_8-C_{18} saturated) will be carcinogenic in humans.

Oral exposure to soaps is generally self-limiting because the taste of soap is easily recognized and unpleasant. In addition, ammonium soap salts have an ammonia odor that is limiting. Because of their strong soil adsorption and the rapid degradation they are not expected to reach surface water via runoff nor are they expected to leach into ground water.

Ammonium salts of fatty acids have the potential to cause dermal, eye, and inhalation effects. However, due to the vapor pressure and the unlikelihood of fatty acid forming aerosol particulates the anticipated risk from the inhalation route of exposure is not expect to cause adverse harm to occupational and residentially exposed individuals. Dermal and ocular exposure is expected to be negated by the use of personal protective equipment (e.g. chemical resistant gloves, goggles, face shield, etc).

Fatty acids are an essential component of the mammalian diet and the body is able to metabolize these soap salts and use them as an energy source. Due to the self limiting nature of these chemicals, their natural occurrence in the environment, their rapid environmental degradation, and their presence in commonly eaten foods (both naturally and intentionally added) the anticipated exposure from the use of ammonium salts of fatty acids as inert ingredients in pesticide products is expected to be minimal and is not anticipated to significantly increase the overall exposure to all populations including infants and children.

Ammonium salts of fatty acids are expected to be only minimally toxic to nontarget organisms, with the exception of aquatic invertebrates. “Soap salts of fatty acids are slightly toxic to birds on an acute basis and are practically non-toxic to birds on a dietary basis, slightly toxic to fish, and highly toxic to aquatic invertebrates”.(EPA Memorandum: Jones, 2006) Appropriate precautionary labeling stipulating the product is hazardous to aquatic invertebrates and that the product should not be used on or near water bodies, where surface water is present, or to intertidal areas below the mean high water mark will further minimize potential exposure and mitigate risk to humans and aquatic organism.

It is highly unlikely that concentrations needed to invoke a toxic response would be reached from the use of ammonium salts of fatty acids (C_8-C_{18} saturated) as inert ingredients in pesticide products; therefore, the Agency believes that there is a reasonable certainly of no harm to human health and the environment. Hence, an exemption from the requirement of tolerance has been

granted under 40 CFR 180.910 for ammonium salts of fatty acids (C_8-C_{18} saturated).

I. BACKGROUND AND USES

On August 12, 2008 Falcon Lab, LLC, 1103 Norbee Drive, Wilmington, DE 19803, submitted a petition to amend 40 CFR 180.910 (Inert ingredients used pre- and post-harvest) by establishing an exemption from the requirement of a tolerance for ammonium salts of fatty acids (C_8-C_{18} saturated), (see Table 1 for chemical name and CAS Reg No.) as inert ingredients in pesticide products on all food commodities.

Table 1- Chemical Name and CAS Reg. No. for Ammonium Salts of Fatty Acids C_8-C_{18} (saturated)

Chain length	CAS Reg. No	Name
Saturated		
C8	5972-76-9	Ammonium caprylate or ammonium octanoate
C9	63718-65-0	Ammonium nonanoate
C10	16530-70-4	Ammonium decanoate
C11	32582-95-9	Undecanoic acid, ammonium salt
C12	2437-23-2	Ammonium laurate or Dodecanoic acid, ammonium salt
C13	191799-95-8	Tridecanoic acid, ammonium salt
C14	16530-71-5	Ammonium myristate
C15	93917-76-1	Ammonium pentadecanoate
C16	5297-93-8	Ammonium palmitate
C17	94266-36-1	Ammonium heptadecanoate
C18	1002-89-7	Ammonium stearate

Ammonium salts of fatty acids are mineral salts of naturally occurring fatty acids. Fatty acids play a significant role in the normal diet of humans, animals and plants. They are naturally present in commonly eaten fats and oils, accounting for approximately 30-40% of the caloric intake in the U.S. diet (~ 90 grams/day). (EPA RED: Soap Salts, 1992; EPA Memorandum: Boyle, 2003) Additional exposure to fatty acids may come from a wide variety of sources, including (but not limited to) FDA-approved uses as direct food additives (2l CFR 172.860; 21 CFR 172.862; and 21 CFR 172.863), in food packaging products (21 CFR 176.200), or through their use in cosmetics. These fatty acids are also used as a waterproofing agent for concrete, stucco, paper and textiles. Currently, they are approved as active and inert ingredients in pesticide product formulations.

Ammonium stearate (C_{18} saturated; CAS Reg. No. 1002-89-7), one of the soap salts, has been approved as an inert ingredient under 40 CFR 180.910 since 1962 for use in pesticide products applied to growing crops or to raw agricultural commodities after harvest. A document published in July of 2002 by the Environmental Protection Agency's Inert Ingredient Focus Group (IIFG) illustrated the reassement of the 40 CFR 180.910 classification and determined

that a reasonable certainty of no harm will result to the general population and to infants and children from the aggregate exposure to residues of ammonium salts of fatty acids (C_8-C_{18} saturated and C_{18} unsaturated). (EPA Memorandum: Boyle and Leifer, 2002)

According to the EPA's "IIFG Decision Documents on Reassessment of Exemptions from Tolerance for Various Salts of Stearic Acid" (2002), in 1974 the Food and Agriculture Organization/World Health Organization (FAO/WHO) published the "Toxicological Evaluation of Certain Food Additives with a Review of General Principles and of Specifications". This evaluation addressed numerous chemicals including ammonium, calcium, and magnesium stearate as anticaking agents in food. As a result of the evaluation, a "not limited" ADI (acceptable daily intake) classification was applied to ammonium, calcium and magnesium stearate as anticaking agents. Furthermore, the report summary states that "stearic acid and [their] salts are normal products of the metabolism of fats and their metabolic fate is well established. Provided the contribution of the cations does not add excessively to the normal body load, there is no need to consider the use of these substances in any different light to that of dietary fatty acids."

In 1982 the EPA approved an exemption from the requirement of tolerance for ammonium and potassium salts of fatty acid when used as pesticide active ingredients on food commodities; however, formal notice was not provided in the Federal Register. That same year, a safety assessment of ammonium stearate by an expert panel of the Cosmetic Ingredient Review (CIR) was published in the Journal of the American College of Toxicology. Acute oral, dermal, skin irritation, teratology and mutagenicity studies were evaluated. The review concluded that these materials are "safe as cosmetic ingredients in the present practices of use and concentration." The use concentration of ammonium stearate in cosmetic products varies from 0.1 to nearly 50 percent. (EPA Memorandum: Boyle and Leifer, 2002).

In 1992 EPA issued a Reregistration Eligibility Document (RED) on soap salts which evaluated two chemically-similar pesticide active ingredients: potassium salts of fatty acids (C_{12}-C_{18} saturated and C_{18} unsaturated) and ammonium salts of fatty acids (C_8-C_{18} saturated and C_{18} unsaturated). The Agency RED for soap salts treats ammonium salts of fatty acids (C_8-C_{18} saturated and C_{18} unsaturated) as one active ingredient. This document also made the finding that all compounds, as defined within these two classes of active ingredients (ammonium soap salts and potassium soap salts), are similar in regard to chemistry, toxicology, and environmental fate and effects. It was determined that all registered pesticide products containing the active ingredient soap salts are not likely to cause unreasonable adverse effects in people or the environment and were eligible for reregistration.

Ammonium soap salts of fatty acids were approved in 2006 as active ingredients in non-food use pesticide products for the suppression and control of a wide variety of undesirable grasses and weeds. Previously, ammonium salts of fatty acids had been registered for other non-food uses, including repelling rabbits and deer from forage and grain crops. (73 FR 39264, July 9, 2008) They also have some insecticidal properties.

In July 2008, 40 CFR 180.1284 established an exemption from the requirement of a tolerance for residues of the active ingredient ammonium salts of higher fatty acids ($C_{8-}C_{18}$ saturated and $C_{8-}C_{12}$ unsaturated) in or on all food commodities when applied for the suppression and control of a wide variety of grasses and weeds. According to the final rule (73 FR 39264, July 9, 2008), "All soap salts with fatty acids having aliphatic carbon chains lengths in the range between C_8 and C_{18} saturated are virtually identical in regard to chemistry and toxicology".

A comprehensive risk assessment conducted by the Human and Environmental Risk Assessment (HERA) on fatty acid salts which included a "Human Health Risk Assessment" (2002) and an "Environmental Risk Assessment" (2003) specifically addressed sodium and potassium salt of fatty acids (even numbered, straight C chains with 10 to 22 C atoms, with C_{16}-C_{22} fatty acid chains having saturated or unsaturated with a C-C double bond) when used as ingredients in European household cleaning products. Although the HERA assessment only evaluates sodium and potassium fatty acid salts, the Soap Salts RED (EPA, 1992) considers potassium and ammonium fatty acid salts to have similar chemistry, toxicology, and environmental fate and effects and is therefore relevant to this assessment. (EPA Memorandum: Jones, 2006)

The HERA document estimated that approximately 71,306 tons of fatty acid soap salts were used annually in household cleaning products (including fabric washing products, fabric conditioners, laundry additives, and surface and toilet cleaners) in Europe. This widespread use results in frequent, regular, and continuous human and non-target organism exposure. The HERA document concluded:

> Fatty acid salts are of low acute toxicity. Their skin and eye irritation potential is chain length dependent and decreases with increasing chain length. They are not skin sensitizers. The available repeated dose toxicity data demonstrate the low toxicity of the fatty acids and their salts. Also, they are not considered to be mutagenic, genotoxic or carcinogenic, and are not reproductive or developmental toxicants.

II. PHYSICAL AND CHEMICAL PROPERTIES

Fatty acids are naturally occurring acids found in fats and oils. A fatty acid is made up of a long chain of hydrogen and carbon atoms, with an extra hydrogen atom at one end and a "carboxyl group" (made up of two oxygen, one

hydrogen and one carbon atom) on the other end. Fatty acids can be "saturated" or "unsaturated". They differ in how they are bound to hydrogen. A saturated fatty acid is one where the carbon atoms are bonded with single bonds; each sharing one set of electrons. As a result, saturated fatty acids have two hydrogen atoms for each carbon atom. Unsaturated fatty acids, on the other hand, have at least one double bond where one set of carbon atoms is bonded by sharing two sets of electrons, instead of each being connected to a hydrogen atom.

When a particular fatty acid reacts with a base such as ammonia, a fatty acid salt is formed which is also referred to as an ammonium soap salt. In other words, soap is essentially a fatty acid salt. The type of fatty acid and length of the carbon chain determines the unique properties of various soap salts.

In general ammonium salts of fatty acids are slightly soluble in water and do not form aerosol particulates. The longer the fatty acid chain the more insoluble it is. The hydrocarbon chain is non-polar and hydrophobic. The "salt" end of the soap molecule is ionic and hydrophilic. Ammonium salts of fatty acids have a vapor pressure near that of water and do not readily vaporize. Ammonium stearate (C_{18} saturated), for example, has a water solubility of 0.56 mg/L and a vapor pressure of 2.5×10^{-8} mmHg at 25° C. It binds strongly to soils (Koc greater than 10) and the log n-octanol-water partition coefficient is above 5. (EPA Memorandum: Boyle and Leifer, 2002)

III. METABOLISM/PHARMACOKINETICS

The 2002 HERA document makes the claim that:

> The acid and alkali salt forms of the same chemical are expected to have many similar physicochemical and toxicological properties when they become bioavailable; therefore, data read across is used for those instances where data are available for the acid form but not the salt, and vice versa. This position is based on experimental studies that have clearly demonstrated a high degree of similarity between the toxicokinetics and toxicodynamics of acid and salt forms of the same chemical (BASF, 2001). A general premise in regulatory toxicology is that testing an acid form of a chemical is representative of the testing that chemical as an alkali salt.

Exposure to ammonium stearate, for example, would likely result in dissociation in the body into the free fatty acid (stearic acid) and the ammonium cation. (EPA Memorandum: Boyle and Leifer, 2002)

Fatty acids are found in commonly eaten fats and oils. Once fats and oils are consumed, the triglycerides are rapidly hydrolyzed in the human body into glycerol and free fatty acids. (EPA Memorandum: Boyle and Leifer, 2002) Fatty acids are normally metabolized by the cells, where they are oxidized to simple compounds for use as energy sources and as structural components utilized in all living cells. Ammonium is also a normally part of the body's metabolism and electrolyte balance.

A 2002 reassessment document on various salts of stearic acid written by the Agency's Inert Ingredient Focus Group describes some of the properties of ammonium stearate:

> Ammonium stearate salts dissociate to form the positively charged ammonium ion (NH_4^+). Nitrogen, a component of the ammonium ion, is an important element in human metabolism, but humans cannot convert atmospheric nitrogen to any form that can be used as part of any of the various metabolic cycles. As a result, nitrogen has to enter the body through the diet by consumption of nitrogen-containing amino acids in protein…Generally the body works to maintain a balance of nitrogen intake and nitrogen excretion. The estimated daily ammonia intake through food and drinking water is 18 mg. In contrast, 4000 mg of ammonia per day are produced endogenously in the human intestine. Ammonia and the ammonium ion are integral components of normal human metabolic processes...The liver converts ammonia via the urea cycle into urea. According to FDA, "the normal liver so readily detoxifies ammonium ion from alimentary sources that blood concentrations of ammonium salts do not rise to the levels necessary to evoke toxic response." Approximately 80% of the body's excess nitrogen is eliminated through the kidneys as urea, approximately 25 to 30 grams per day.

IV. TOXICOLOGY

The Agency's Reregistration Eligibility Document (RED) for Soap Salts (1992) treats ammonium salts of fatty acids (C_8-C_{18} saturated and C_{18} unsaturated) as one active ingredient. The document covered both ammonium salts of fatty acids and potassium salts of fatty acids and makes the conclusion that all compounds, as defined within these two classes, are similar in regard to chemistry, toxicology, and environmental fate and effects. This document utilizes information on ammonium and potassium soap salts and their free fatty acids.

Acute Oral and Dermal

According to the 1992 RED, soap salts have low acute oral and dermal toxicity. Ammonium stearate (C_{18} saturated), for example, has an acute oral LD_{50} of >5 g/kg (rat) and an acute dermal LD_{50} of >3g/kg (guinea pig). Pelargonic acid (Nonanoic acid), a C_9 saturated fatty acid, showed an acute oral LD_{50} of >5g/kg and an acute dermal LD_{50} of >2g/kg (animal not identified; test material-60% pelargonic acid emulsifiable concentrate). Similarly, the oral LD_{50} of oleic acid (C_9 unsaturated) in rats was 74 g/kg. According to the Agency's acute toxicity catagories (40 CFR 156.62) ammonium soap salts are classified as category IV via the oral route and category III via the dermal route.

Acute Inhalation

There were limited data available regarding inhalation of fatty acids, and none available regarding inhalation of fatty acid salts. Since fatty acid salts are known eye and skin irritants, it is highly likely that they will also be strongly irritating via the inhalation route of exposure. One study exposed male and

female albino rats to pelargonic acid (nonanoic acid) for 4 hours. This study reported an LC_{50} of 1.244 milligrams/liter (mg/L). (MRID 43843503)

Dermal Irritation

Several studies were outlined in the 1992 RED document on soap salts,

> On human skin 2.5mg of soap for 24 hours caused moderate irritation; and 10 mg of soap on rabbit skin caused mild irritation. On human skin, 11,800 mg of the potassium salt of palmitic acid was irritating. For the potassium salt of caprylic acid, 7320 mg was irritating on human skin. Stearic acid was mildly irritating to human skin when 75 mg was applied intermittently for 3 days. On rabbit skin, 500 mg of stearic acid applied for 24 hours was moderately irritating. Oleic acid was moderately irritation to human skin when 15 mg was applied intermittently for 3 days; and mildly irritating to rabbit skin when 500mg was applied.

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Skin Sensitization and Eye Irritation

Ammonium soaps of higher fatty acids may cause allergic skin reactions in some individuals; however, the Agency believes allergic reactions are uncommon and transient. Soap salts are not classified as skin sensitizers. Ammonium soap salts are irritating to the eyes and may cause permanent eye damage. (US EPA RED: Soap Salts, 1992)

Repeat dose

A 14-day range finding study (MRID 43843507, 1995) conducted on male and female rats given nonanoic acid in their diet at doses up to 1,834 mg/kg/day found no significant effects in regards to survival, clinical signs, body weight gain, food consumption, hematology (red or white cell counts, hematocrit, or hemoglobin), clinical chemistry (glucose, triglycerides, total protein, albumin, blood urea nitrogen, creatinine, and alanine aminotransferase (ALT)) or gross pathology. Minor changes were detected in two of the serum chemistry parameters, but neither of these is considered toxicologically significant nor are they likely to represent an important risk factor in potential human exposure.

In the July 9, 2008 Final Rule (73 FR 39264) establishing an exemption from the requirement of tolerance for ammonium salts of higher fatty acids (C_8-C_{18} saturated) the Agency concluded that a 90-day oral toxicity study was not necessary for a dietary risk assessment. The decision was based on the lack of effects at extremely high doses in the range finding study, the natural occurrence of these fatty acids in nature, the results from the acute mammalian toxicology studies, and the unlikelihood of prolonged human exposure via the oral route due to the proposed use patterns.

Endocrine

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally-occurring estrogen, or other such endocrine effects as the Administrator may designate". Ammonium salts of fatty acids (C_8-C_{18} saturated) are not known endocrine disruptors nor are they or their metabolites related to any class of known endocrine disruptors.

Mutagenicity/Genotoxicity

According to the 1992 RED, 600 µmol/L of the sodium salt of caprylic acid, tested on guinea pig kidney cells, showed DNA inhibition. Unscheduled DNA synthesis occurred in mouse cells treated with 35 mg/kg of oleic acid (C9 unsaturated). Cytogenetic analysis was positive for hamster fibroblasts treated with 2500 µg/L of oleic acid and for Saccharomyces cerevisiae treated with 100 mg/L oleic acid.

Studies on pelarogonic acid; however, showed that it was non-mutgenic when evaluated using the Ames test (Salmonella/reverse mutation assay). Negative results were also seen when in vivo cytogenetics testing was done using micronucleus assay. In a mouse lymphoma forward mutation study, pelargonic acid appears to induce a weak mutagenic response at concentrations equal to or greater than 50 milligrams/milliliter (mg/mL). This was observed in the presence of increasing toxicity, and may be an indication of gross chromosomal changes or damage and not actual mutational changes within the thymidine kinese gene locus.”(68 FR 7931, February 19, 2003)

Ammonium salts of fatty acids are not believed to be mutagenic. When used at high doses, reproductive and mutagenic effects were observed in laboratory animals given potassium salts of coco fatty acids; however, studies on one of the ammomium salts, pelargonic acid (nonanoate acid), did not show developmental or mutagenic effects. Due to the low toxicity of these salts, the lack of mutagenicity, and the anticipated exposure from the use of these chemicals as inert ingredients in pesticide products the Agency does believe ammonium salts of fatty acids (C_8-C_{18} saturated) will be carcinogenic in humans.

Reproduction/ Developmental

The Soap Salts RED (citing, NIOSH 1987 Registry of Toxic Effects of Chemical Substances) notes that potassium salts of coco fatty acid, when administered to lab animals at high doses, can cause reproductive effects. Effects on post-implantation mortality were seen in mice given 6 g/kg on days 2-13 of pregnancy and musculo-skeletal abnormalities were observed at doses of 600 mg/kg.

A developmental toxicity study in rats (MRID 43843508) on pelargonic acid (nonanoate acid) showed no adverse effect of treatment on clinical signs, body weights, weight gain, or food/water consumption. Female rats were gavaged on gestation days 6-15. No fetal toxicity attributed to the effects of treatment was observed between the treated or the untreated controls. Evaluated parameters included survival, clinical signs, body weight data, food and water consumption data, gross examination of maternal tissues, uterine examination for embryo/fetal implantation data, fetal weight and crown-rump length data, and fetal evaluations (external, visceral, and skeletal). The mean number of viable fetuses, early or late resorptions, implantation sites, corpora lutea, pre- and post-implantation losses, sex ratios, and fetal body weights were comparable to those of the control group. The no observed effect level (NOEL) for maternal and developmental toxicity was 1,500 mg/kg/day with the lowest observed toxicity level (LOEL) greater than 1,500 mg/kg/day.

Neurotoxicity

Although a neurotoxicity study was not performed, no evidence of neurotoxicity was observed in any of the studies at doses up to 1500 mg/kg. The Agency concluded that ammonium salts of fatty acids are not neurotoxic.

Special Consideration for Infants and Children (FQPA Safety Factor)

FFDCA section 408 provides that EPA shall apply an additional tenfold margin of exposure (safety) for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base unless EPA determines that a different margin of exposure (safety) will be safe for infants and children. There was no evidence of systemic toxicity or developmental toxicity at doses up to 1500 mg/kg/day in a developmental toxicity study in rats. No systemic toxicity was observed at doses up to and including 1837 mg/kg/day in a 14-day toxicity study in rats. Since there is no hazard identified to adults and developing fetuses a quantitative FQPA assessment was not performed. In addition, the Agency has previously concluded that there is a reasonable certainty that no harm to the U.S. population, including infants and children, will result from aggregate exposure to residues of ammonium salts of fatty acids (C_{8}-C_{18} saturated) due to their use as active ingredients in pesticide formulations. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

Although residue data is not required for a tolerance exemption it is anticipated that the residues on food will be low due to the limiting nature of the chemical in food use products (e.g. palatability and herbicidal properties). Moreover, fatty acids are part of the human diet and the exposure resulting from the use of these soap salts in pesticide formulation are not expected to exceed the levels of naturally occurring fatty acids in commonly eaten foods.

V. ENVIRONMENTAL FATE AND DRINKING WATER

Ammonium salts of fatty acid are not likely to persist in the environment and are expected to be indistinguishable from naturally occurring ammonium ions and fatty acids already present in the environment as a result of plant metabolism and formation by soil microbes (EPA Memorandum: Jones, 2006). The expected half-life of these fatty acids is less than one day. They adsorb strongly to soil and sediment and are rapidly degraded by microbial organism. Microbial degradation biotransforms fatty acids by oxidative cleavage of the carbon chain. Both the rate of metabolism and the solubility of the fatty acid soap salt increases with decreasing C chain length (HERA, 2003).

Because of their strong soil adsorption and the rapid degradation of ammonium salts of fatty acids they are not expected to reach surface water via runoff nor are they are expected to leach into ground water. Based on the physical/chemical properties, volatilization from soils and water is not expected. There is no expected translocation into plants. (Health Canada, 2008)

According to the Agency's 2002 document entitled 'Reassessment of Exemptions from the Requirement of a Tolerance for Various Salts of Stearic Acid" (including ammonium stearate):

> Although the potential to bioaccumulate is high, bioavailability is offset by the tendency to adsorb strongly to soil and sediment particulates. However, concentration at the water-air interface is likely to be higher than in the water column, which results in lowering the surface tension of the aqueous system. The lowering of the surface tension and the hydrophobic layer at the water-air interface has the potential to alter the physical and chemical characteristics of the aquatic environment.

VI. EXPOSURE ASSESSMENT

A. Exposure Profile

The primary route of residential exposure to ammonium salts of fatty acids when used as inert ingredients in pesticide formulations is through oral exposure to food. However, the levels of ammonium salts of fatty acids is not expected to exceed the concentration of naturally occurring or intentional added fatty acids in commonly consumed foods. Based on the natural presence of these compounds in the environment, the body's ability to metabolize them, and their low toxicity, a qualitative approach has been used to assess exposure.

According to the RED, oral exposure to soaps is generally self-limiting because the taste of the soap is easily recognizable. In addition, ammonium soap salts have a notable ammonia odor that is also limiting. Dietary exposure would be further minimized via plant metabolism of the chemical through oxidative pathways. (73 FR 39264, July 9, 2008) Ammonium salts are not expected to enter drinking water because of the high binding capability of these

salts to soil and the lack of persistence due to the rapid microbial degradation of the chemical.

Although dermal exposure would be possible, the low toxicity of the chemical and the use of personal protective equipment, as would be expected with the registration of a pesticide formulation containing this inert ingredient, the Agency concluded that the effect from dermal exposure will be low. Ammonium salts of fatty acids are irritating to eye and therefore, protective eye wear would be necessary to negate the potential for permanent eye damage. Non-occupational inhalation exposure is not expected because ammonium salts of fatty acids do not form aerosol particulates, have a vapor pressure near that of water, and do not readily vaporize. (73 FR 39264, July 9, 2008)

Occupation exposure is possible; however, due to the low toxicity of the chemical and the use of personal protective equipment, the Agency concluded that the risk to workers will be minimal.

B. Aggregate Exposure

Section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) directs the Agency to evaluate aggregate exposure from "pesticide chemical residue and to other related substances, including dietary exposure under the tolerance and all other tolerances in effect for the pesticide chemical residue, and exposure from other non-occupational sources". The expected exposure pathway for ammonium salts of fatty acid is through the oral and the dermal routes of exposure.

Ammonium salts of fatty acids have been granted an exemption from tolerance as an active ingredient under 40 CFR 180.1284 in food use products. They have also been registered for non-food use as a repellant for rabbits and deer from forage and grain crops. (73 FR 39264, July 9, 2008)

In addition to exposure from naturally occurring fatty acids, exposure to fatty acids may come from a wide variety of sources, including (but not limited to) FDA-approved uses as food additives (*2l CFR 172.860; 21 CFR 172.862; and 21 CFR 172.863),* in food packaging products, or through their use in cosmetic products. (EPA Memorandum: Boyle, 2003)

Because of the low oral and dermal toxicity, the rapid degradation of the chemical, and the natural presence of fatty acids in the environment, the Agency concluded that aggregate exposure will result in minimal risk to all subpopulation including infants and children. Since the inhalation route is not a likely exposure pathway the anticipated risk from inhalation exposure is also considered minimal. (July 9, 2008, 73 FR 39264)

C. Cumulative Exposure

Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The fatty acid salts are structurally related; however, all are low toxicity chemicals. Therefore, the resultant risks separately and/or combined should also be low. In addition, the rapid environmental degradation and the body's ability to utilize these fatty acids as a natural part of the diet further supports the Agency's findings that, based on available information, there is no concern from cumulative effects of ammonium salts of fatty acids (C_8-C_{18} saturated) and other substances with a common mechanism of toxicity.

VII. RISK CHARACTERIZATION

In addition to naturally occurring fatty acids found in the environment and commonly consumed foods, ammonium salts of fatty acids are used as food additives and in food packing products, cosmetics, and have been previously approved by the EPA for use in pesticide formulations both as active and inert ingredients. They have proven to be of low toxicity via the oral and dermal routes of exposure. When applied for long periods of time, they have the potential to be dermal irritants. Allergic skin reactions may occur in some individuals; however, the Agency concluded that allergic reactions are uncommon and transient. Soap salts are not classified as skin sensitizers.

Studies have shown ammonium salts of fatty acids are eye irritants and have the potential to cause permanent eye injury. Although there is limited data available regarding the inhalation of soap salts they are anticipated to be strongly irritating via the inhalation route of exposure because of their known eye and skin irritation potential; therefore, it is highly likely that they also will be strongly irritating via the inhalation route of exposure.

Due to the low toxicity of these soap salts and the natural occurrence of fatty acids in the environment and food products, a chronic study was not required. A 14-day range finding study did not produce any significant effects of nonanoic acid (C_9 saturated) given to rats at doses up to 1,834 mg/kg/day. Ammonium salts of fatty acids are not believed to be mutagenic. When used at high doses, reproductive and mutagenic effects were observed in laboratory animals given potassium salts of coco fatty acids; however, studies on one of the ammomium salts, pelargonic acid (nonanoate acid), did not show developmental or mutagenic effects. Due to the low toxicity of these salts, the lack of mutagenicity, and the anticipated exposure from the use of these chemicals as inert ingredients in pesticide products the Agency does not believe ammonium salts of fatty acids (C_8-C_{18} saturated) will be carcinogenic in humans.

Ammonium salts of fatty acids have the potential to cause dermal, eye, and inhalation effects. Due to the vapor pressure and the unlikelihood of fatty acid forming aerosol particulates, the anticipated risk from the inhalation route of exposure is not expect to cause adverse harm to occupational and residentially exposed individuals. Dermal and ocular exposure is expected to be negated by the use of personal protective equipment (e.g. chemical resistant gloves, goggles, face shield, etc).

According to the 1992 EPA RED on soap salts, oral exposure to soaps is generally self-limiting, because the taste of soap is easily recognized and unpleasant. In addition, ammonium soap salts have an ammonia odor that is limiting. Because of their strong soil adsorption and the rapid degradation of ammonium salts of fatty acids they are not expected to reach surface water via runoff nor are they expected to leach into ground water. Due to the self limiting nature of these chemical and their natural occurrence in the environment it is highly unlikely that concentrations needed to invoke a toxic response would be reached; therefore, the Agency believes that there would not be any reproductive or mutagenic effects for this inert ingredient.

Fatty acids are an essential component of the mammalian diet and the body is able to metabolize these soap salts and use them as an energy source. Because of their natural occurrence in the environment, their rapid environmental degradation, and their presence in commonly eaten foods (both naturally and intentionally added) the anticipated exposure from the use of ammonium salts of fatty acids as inert ingredients is expected to be minimal and is not anticipated to significantly increase the overall exposure to all populations including infants and children.

Ammonium salts of fatty acids are expected to be only minimally toxic to nontarget organisms, with the exception of aquatic invertebrates. “Soap salts of fatty acids are slightly toxic to birds on an acute basis and are practically non-toxic to birds on a dietary basis, slightly toxic to fish, and highly toxic to aquatic invertebrates”. (EPA Memorandum: Jones, 2006) Appropriate precautionary labeling of end use products containing ammonium soap salts will further minimize potential exposure and mitigate risk to humans and nontarget organisms.

VIII. ECOTOXICITY AND ECOLOGICAL RISH CHARACTERIZATION

Evaluation of the ecotoxicity of ammonium salts of fatty acids was previously performed by the Agency and has been outlined in the 1992 RED on Soap Salts and the 2006 Biopesticide Registration Action Document (BRAD) on ammonium nonanoate. It was determined that ammonium soap salts are slightly toxic to birds on an acute basis and are practically non-toxic to birds on a dietary basis (see Table 2). Although the study used a test substance that was only 14.65% pure, the Agency feels that the exposure to bird species will not be

significantly greater than the natural occurrence of fatty acids in the environment. In addition, the avian diet calls for fatty acids; therefore, mechanisms are in place to metabolize these chemical in the body. Based on this information the Agency does not feel there is increased risk to birds or other terrestrial animals.

Ammonium salts of fatty acids are slightly toxic to fish and highly toxic to aquatic invertebrates (see Table 2). Ammonium salts of fatty acids are readily biodegradable and are rapidly metabolized by soil microorganisms (half-life < 1 day) and; therefore, are not expected to persist in the environment. Because the product is not intended for direct application to aquatic sites, exposure to aquatic organisms (fish and invertebrates) is further mitigated.

As would be expected for a herbicide, ammonium soap salts of fatty acids are toxic to freshwater algae and aquatic plants. However, based on the intended use pattern (will not be applied directly to water, areas where surface water is present, or to intertidal areas below the mean high water mark) and the high soil binding properties of these salts, it is not expected that ammonium soap of fatty acids will enter aquatic systems; therefore, risk to aquatic plants and algae is expected to be negligible. (Health Canada, 2008)

In addition to their herbicidal properties, soap salts also have insecticidal properties. There are relatively selective in toxicity based on the insect species and stage of development. Soft-bodied insects such as aphids, whiteflies, and mealybugs are more susceptible to desiccation. Insects with more durable exteriors such as ladybird beetles are least effect whereas insects in the immature, flightless stage of development are more vulnerable to the effects of this the chemical ingredient. (NPTC, 2001) The exposure to insects from the use of ammonium salts of fatty acids as inert ingredients in pesticide formulations is expected to be low.

Table 2: Non-target Organism Data from the Soap Salts RED (EPA, 1992)

Data Requirement	LD50\LC50\EC50	Test Material	Toxicity Category	Citation
Avian Acute Oral Toxicity OPPTS 850.2100	>2150 mg/kg (bobwhite quail)	14.65% pure	Slightly toxic	MRID 41767112
Avian Dietary Toxicity OPPTS 850.2200	>5000 mg/kg (bobwhite quail & mallard duck)	14.65% pure	Practically non-toxic	MRID 41767113, -14
Acute Fish Toxicity OPPTS 850.1075	96-hr: 18.06 mg/L (rainbow trout) 96 hr: 35.35 mg/L[1] (bluegill sunfish)	Potassium salt technical grade	Slightly toxic	EPA. (1992)
Aquatic Invertebrates OPPTS 850.1010	48 hr: 0.57 mg/L (*D. magna*)	Potassium salt technical grade	Highly toxic	MRID 400662-00
Non-Target Plants OPPTS 870.2500	No data available for any soap salt but product is also use as a terrestrial herbicide	-	-	-

1 potassium soap salt used; considered by the Agency to be equivalent to ammonium soap salt for ecorisk assessment purposes (EPA, 1992).
2 sodium decanoate (C_{10} fatty acid salt) was test substance.

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